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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,692	08/25/2000	J. Oliver Dolly	17311(AP)	6378

7590 03/25/2004

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2525 Dupont Drive
Irvine, CA 92612.

EXAMINER	
BUGAISKY, GABRIELE E	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/648,692	DOLLY ET AL.	
	Examiner	Art Unit	
	Gabriele E. BUGAISKY	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/10/2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/2000* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

The election of Group II in the response of 10/16/2003 and cancellation of non-elected claims is noted. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

The information disclosure statement filed 4/19/2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. No copy of the Borodic et al. (AX) reference was received; two copies of references AY and AZ were however supplied.

Please note that the first author of reference BC is Hutchinson, not Smith, the last listed author. The citation has been corrected on the PTO1449.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specification

The abstract of the disclosure is objected to because the first sentence contains no verb. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities:

Page 14, line 4 recites "TeT%X". Is this supposed to be "TeTx"?

Page 24, line 1 recites "calmodilin". Is this supposed to be "calmodulin"?

It also is not readily apparent whether "TeNT" (e.g., page 2, line 10), "TxNT" (e.g., p 3, line 17) and "TeTx" (e.g., page 6, line 7) are the same molecule. The only one, which appears identified by a full name, is TeNT.

Appropriate correction is required.

This application does not fully comply with 37 C.F.R. 1.821-1.825 as not all recitations of sequences show are followed by the corresponding SEQ ID Nos. (e.g., page 18, lines 19-20; page 20, lines 24-25; page 27, line 24; page 37, lines 18, 19, 22; etc.)

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademarks "TWEEN" (e.g., page 34, line 5) and "TALON" (e.g., page 50, line 17) has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 32 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, the claim has been further treated on the merits only to the extent possible.

Claim 26 is objected to because of the following informalities: "either of claims 20 or 23" should be: "either of claim 20 or 23". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim depends from a cancelled claim and is therefore indefinite. There also is no antecedent basis for "said binding tag". The claim is also incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: what purification steps occur after the specific binding complex is formed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 20-33 are rejected under 35 U.S.C. 102(b) as being anticipated by WO98 /07864 (Shone *et al.*) The reference provides for recombinant plasmids comprising single chain peptides from clostridial neurotoxins: The abstract states e.g.,

> " The polypeptide thus combines useful properties of a clostridial toxin, such as a botulinum or tetanus toxin, without the toxicity associated with the natural molecule. The polypeptide can also contain a third domain that targets it to a specific cell, rendering the polypeptide useful in inhibition of exocytosis in target cells."

It provides on page 19 lines 1-5 a plasmid comprising a sequence encoding a single chain of a clostridal heavy chain (LC) (which contains a binding element to a target cell surface marker and a translocation element) and a clostridial light chain, fused to a glutathione S- transferase binding tag. It also provides a plasmid variant incorporating a protease cleavage site (for Factor Xa) on page 20, lines 2-10. Additionally, it provides plasmids variants which encode specific binding activities including IGF-1, the terminal 14 amino acids of CtxA, and a IgG binding domain (page 20. The inventors further engineer a sequence coding for a protease cleavage site located between the end of the clostridial heavy chain sequence and the sequence coding for the binding ligand. Expression of this gene produces a polypeptide which has the desired protease sensitivity at the interface between the domain providing H.sub.N function and the binding domain. Such a modification enables selective removal of the C-terminal binding domain by treatment of the polypeptide with the relevant protease. (page21, lines 1-6). It is taught on page 21, lines 7-26 that such binding domains can be incorporated into any of the polypeptide sequences , that binding domains could be incorporated at any appropriate location and that one may provide a desired protease cleavage site at a desired location., so long as the polypeptide retains domains having the properties required by the invention. By providing the genetic

variants which incorporate the recited subject matter of the instant claims, Shone et al anticipates the instant invention.

Claims 20-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Shone *et al.*(US patent 6461617.) The reference provides for recombinant plasmids comprising single chain peptides from clostridial neurotoxins: The abstract states e.g.,

> " The polypeptide thus combines useful properties of a clostridial toxin, such as a botulinum or tetanus toxin, without the toxicity associated with the natural molecule. The polypeptide can also contain a third domain that targets it to a specific cell, rendering the polypeptide useful in inhibition of exocytosis in target cells."

It provides in column 10 lines 15-20 a plasmid comprising a sequence encoding a single chain of a clostridal heavy chain (LC) (which contains a binding element to a target cell surface marker and a translocation element) and a clostridial light chain, fused to a glutathione S- transferase binding tag. It also provides a plasmid variant incorporating a protease cleavage site (for Factor Xa) in column 11, lines 23-34. Additionally, it provides plasmids variants which encode specific binding activities including IGF-1, the terminal 14 amino acids of CtxA, and a IgG binding domain (column 11, lines 35-52). The inventors further engineer a sequence coding for a protease cleavage site located between the end of the clostridial heavy chain sequence and the sequence coding for the binding ligand. Expression of this gene produces a polypeptide which has the desired protease sensitivity at the interface between the domain providing H.sub.N function and the binding domain. Such a modification enables selective removal of the C-terminal binding domain by treatment of the polypeptide with the relevant protease. (column 11,

lines 52-65. It is taught in column 12, lines 2-24 that such binding domains can be incorporated into any of the polypeptide sequences , that such binding domains could be incorporated at any appropriate location and that one may provide a desired protease cleavage site at a desired location., so long as the polypeptide retains domains having the properties required by the invention. By providing the genetic variants which incorporate the recited subject matter of the instant claims, Shone et al anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-29 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shone et al. (US patent 6461614). The reference is discussed above. It suggests in numerous

places that in additional to the exemplified botulinum toxin, the invention can be practiced with tetanus toxin. (see, e.g., abstract, column 3, line

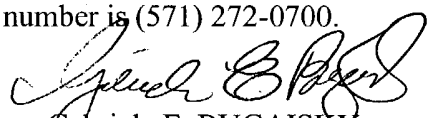
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gabriele E. BUGAISKY whose telephone number is (703) 308-4201; after 1/20/2004, her new number will be (571) 272-0945. The examiner can normally be reached on Tues.- Fri 8:15 AM-1: 45 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher SF Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-0700.



Gabriele E. BUGAISKY
Primary Examiner
Art Unit 1653